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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

SHARAREH, SHAHNAM J

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 03/12/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/763,236

Applicant(s)

FREEMAN ET AL.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/11/2001, 11/25/2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-45 is/are pending in the application.
- 4a) Of the above claim(s) 31 and 33-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-30, 32 and 37-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse for Group I and the species of -NH as the linker, hydrogen as the R1-R3, and alkyl as the R4 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the instant application is directed to "bioactive reductive conjugates" from which a drug is released and that no plurality of invention was raised during the International Phase. This is not found persuasive because the restriction and species, as set forth in Paper no. 8, do not relate to a single inventive concept. Specifically, the Markush species of pending claims are not so linked as to form a single general inventive concept. Each conjugate product identified possesses unique structure to the extent that they do not share a common core.

The election of species requirement is solely based on the lack of a single inventive concept among the groups set forth in claim 29, regardless of their generic claims. Moreover, Applicant has not provided any evidence, now on record, or argued that such species are obvious variants of each other. Applicant also raises the question that the Examiner is not entitled to raise a non-unity objection once the issue has been described in the international phase. In response, the Applicant's attention is drawn to MPEP 1893.03 (d), U.S. National Application Filed Under 35 U.S.C. 371. § 1.499 *Unity of invention during the national stage*. Accordingly:

If the examiner finds that a national stage application lacks unity of invention under § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Such requirement may be made before any action on the merits but may be made at any time before the final action at the discretion of the examiner. Review of any such requirement is provided under §§ 1.143 and 1.144.

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Accordingly, Examiner may raise a lack of unity issue during national stage phase on his discretion. Thus, the requirement for the election of species is also proper.

Claims 31, 33-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10. This application contains claims 31, 33-36 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. The prosecution of the claims is to the extent that reads on the species of – NH as the linker, hydrogen as the R1-R3, and alkyl as the R4.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 30, 37, 39-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The

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Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 37, 41 and 44 respectively recite the broad recitation of anti-infective, arthritic conditions or gastrointestinal disorders, and the claim also recites such agents as antibiotics or such conditions as osteoarthritis or Crohn's disease which is the narrower statement of the range/limitation.

3. Claim 30 is indefinite. It is not clear what type of chemical groups sits on positions Z1-Z4.

4. Claim 39 and all dependent claims thereof are indefinite. The circular limitation of "method of therapeutic treatment comprising administering to a subject in need of such treatment" in claim 39 is vague. It is not clear who is being treated for what. Accordingly, the metes and bound of the claim is not clear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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5. Claims 24-28, 37-45 are rejected under 35 U.S.C. 102(a) as being anticipated by Rauth et al (Int. J. Radiation Oncology boil Phys. Vol 42 No. 4 pp. 755-762 1998).

Rauth teaches bioreductively activated drugs used as antimicrobials, chemotherapeutic agents and radiosensitizers (see abstract, figure 8, specially nitraquine and nitracrine, and figure 5-6). Rauth further describes the utility of such bioreductive drugs. Thus, Rauth anticipates the limitations of the instant claims.

6. Claims 24-28, 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Hay et al (Anti-Cancer Drug Design 1996, IL 383-402).

Hay discloses nitroimidazol alkanoic acids wherein the compound is a bioconjugate comprising an aromatic bioreductive moiety with a nitro group and an active drug, (compounds 4 of Scheme 1, also page 397, Scheme 2, step v). Hay further discloses cyclization of the bioreductive moiety to release the active drug. (see scheme 1). Hay anticipates the limitations of the instant claims.

7. Claims 24-28, 37-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al US Patent 5,652,255.

Adams nitric oxide synthase inhibitors meet the limitations of the instant claims (see col 10, 2nd col, col 14, lines 13-46, col 16, lines 33-60, col 19-20, examples 1-3). Therefore, Adams is anticipatory to the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 24-30, 32, 37-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rauth et al.

The teachings of Rauth et al are described above. The compound of Rauth and the instant compound set forth in claim 29 differ in that Rauth's reductive entity is shorter by one carbon chain. However, it has been held by the Court that "homologs are generally sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563, F2d 457, 195 USPQ 426

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(CCPA 1977). Accordingly, it would have been within the general skill of a worker in the chemical art to make obvious modification within Rauth's compounds, such as adding additional -CH₂-, and maintain its clinical activity.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

ss
March 7, 2003


RUSSELL TRAVERS
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